B3 Cont.

(d) inserting the two different fragments into the vector to form the targeting construct.

5. A murine embryonic stem cell comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene.

6. (Canceled) The cell of claim 5, wherein the cell is a murine cell.

7. (Canceled) The cell of claim 5, wherein the cell is an embryonic stem cell.

8. A transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene wherein said mouse exhibits a phenotype comprising an eye abnormality.

B4 (pbc)

9. A cell derived from the mouse of claim 8.

10. A method of producing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, the method comprising:
(a) introducing the targeting construct of claim 1 into a cell;
(b) introducing the cell into a blastocyst;
(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a cGMP phosphodiesterase gene, the method comprising:
(a) providing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the mouse exhibits a phenotype comprising an eye abnormality; and
(b) administering an agent to the transgenic mouse; and

(c) determining whether the expression of cGMP phosphodiesterase in the transgenic mouse is modulated.

12. A method of identifying an agent that modulates the function of a cGMP phosphodiesterase gene, the method comprising:

(a) providing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene;

(b) administering an agent to the transgenic mouse; and

(c) determining whether the function of the disrupted cGMP phosphodiesterase gene in the transgenic mouse is modulated.

13. A method of identifying an agent that modulates the expression of cGMP phosphodiesterase, the method comprising:

(a) providing a murine cell comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene;

(b) contacting the cell with an agent; and

(c) determining whether expression of the cGMP phosphodiesterase is modulated.

14. A method of identifying an agent that modulates the function of cGMP phosphodiesterase, the method comprising:

(a) providing a murine cell comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene;

(b) contacting the cell with an agent; and

(c) determining whether function of the cGMP phosphodiesterase gene is modulated.

15. (Canceled) The method of claim 13 or claim 14, wherein the cell is derived form the non-human transgenic animal of claim 8.

16. (Canceled) An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. The transgenic mouse of claim 8, wherein the eye abnormality is a retinal abnormality.

18. The transgenic mouse of claim 17, wherein the retinal abnormality is characterized by retinal degeneration or retinal dysplasia.

19. The transgenic mouse of claim 18, wherein the transgenic mouse exhibits an absence of photoreceptor layers.

Sub C1

20. The transgenic mouse of claim 18, wherein the eye abnormality is consistent with vision problems or blindness.

21. The transgenic mouse of claim 18, wherein the retinal abnormality is consistent with retinitis pigmentosa.

B5

Sub C1

22. The transgenic mouse of claim 17, wherein the eye abnormality comprises at least one of the following: thinning or vacuolation of the inner nuclear layer of the eye; thinning of the inner plexiform layer of the eye; loss of ganglion cell nuclei; gliosis of the nerve fiber layer; or attenuation of retinal vasculature.

23. A method of producing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the transgenic mouse comprises an eye abnormality phenotype, the method comprising:

(a) introducing a cGMP phosphodiesterase alpha subunit gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase gene.

24. (Canceled) The transgenic mouse of claim 17, wherein the transgenic mouse is heterozygous for a disruption in an cGMP phosphosdiesterase gene.

25. (Canceled) The transgenic mouse of claim 17, wherein the transgenic mouse is homozygous for a disruption in an cGMP phosphodiesterase gene.

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26. A cell derived from the transgenic mouse of claim 8 or claim 23, wherein the cell comprises a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene.

27. A method of identifying an agent that ameliorates an eye abnormality, the method comprising:

(a) administering an agent to a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene;; and

(b) determining whether the agent ameliorates the eye abnormality of the transgenic mouse.

28. The method of claim 27, wherein the eye abnormality is a retinal abnormality.

29. The method of claim 28, wherein the retinal abnormality is characterized by retinal degeneration or retinal dysplasia.

30. The method of claim 29, wherein the transgenic mouse exhibits an absence of photoreceptor layers.

31. The method of claim 27, wherein the eye abnormality comprises at least one of the following: thinning or vacuolation of the inner nuclear layer of the eye; thinning of the inner plexiform layer of the eye; loss of ganglion cell nuclei in the eye; gliosis of the nerve fiber layer of the eye; or attenuation of retinal vasculature in the eye.

32. A method of identifying an agent which modulates cGMP phosphodiesterase expression, the method comprising:

(a) administering an agent to a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the transgenic mouse comprises a phenotype comprising an eye abnormality; and

(b) determining whether the agent modulates cGMP phosphodiesterase expression in the transgenic mouse, wherein a modulation of the phenotype is indicative of a modulation of cGMP phosphodiesterase expression.

B6 Cont. Cl used

33. A method of identifying an agent which modulates a phenotype comprising an eye abnormality, wherein the phenotype is associated with a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene; and

(b) determining whether the agent modulates the phenotype.

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34. (Canceled) The method of claim 33, wherein the phenotype comprises an eye abnormality.

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35. A method of identifying an agent which modulates a phenotype associated with a disruption in an cGMP phosphodiesterase gene, the method comprising:

B7

(a) administering an agent to a transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase gene, wherein said mouse exhibits an eye abnormality or hyperactivity; and

(b) determining whether the agent modulates the phenotype.

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36. (Canceled) The method of claim 35, wherein the phenotype comprises an eye abnormality.

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37. A method of identifying an agent which modulates cGMP phosphodiesterase expression, the method comprising:

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(a) providing a murine cell comprising a homozygous disruption in cGMP phosphodiesterase alpha subunit gene;

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(b) contacting the cell with an agent; and

(c) determining whether the agent modulates cGMP phosphodiesterase expression, wherein modulation of a phenotypic abnormality comprising an eye abnormality is indicative of an agent that modulates the expression of a cGMP phosphodiesterase gene.

38. (Canceled) The method of claim 37, wherein the phenotype comprises an eye abnormality.

B9

39. A method of identifying an agent which modulates cGMP phosphodiesterase gene function, the method comprising:

(a) providing a murine cell comprising a homozygous disruption in an cGMP phosphodiesterase alpha subunit gene;

(b) contacting the cell with an agent; and

(c) determining whether the agent modulates cGMP phosphodiesterase gene function, wherein modulation of a phenotypic abnormality comprising an eye abnormality is indicative of an agent that modulates the function of a cGMP phosphodiesterase gene.

40. (Canceled) The method of claim 39, wherein the phenotype comprises an eye abnormality.

41. (Canceled) An agent identified by the method of claim 28, claim 33, claim 35, claim 37 or claim 39.

B10

42. A transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase alpha subunit gene, wherein the transgenic mouse exhibits a phenotype comprising hyperactive behavior.

43. (Canceled) The transgenic mouse of claim 42, wherein the transgenic mouse is heterozygous for a disruption in an cGMP phosphodiesterase gene.

44. (Canceled) The transgenic mouse of claim 43, wherein the transgenic mouse is homozygous for a disruption in an cGMP phosphodiesterase gene.

45. A method of identifying an agent that ameliorates hyperactive behavior, the method comprising:

(a) administering an agent to a transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase alpha subunit gene; and

(b) determining whether the agent ameliorates hyperactive behavior of the transgenic mouse.

46. A method of identifying an agent which modulates cGMP phosphodiesterase expression, the method comprising:

(a) administering an agent to the transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene; and

(b) determining whether the agent modulates cGMP phosphodiesterase expression in the transgenic mouse, wherein the agent has an effect on hyperactive behavior of the transgenic mouse.

47. A method of identifying an agent which modulates a phenotype associated with a disruption in a cGMP phosphodiesterase gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene; and

(b) determining whether the agent modulates hyperactive behavior of the transgenic mouse.

48. (Canceled) An agent identified by the method of claim 45, claim 46 or claim 47.